REMARKS

I. Status of the claims

Claims 3 and 5 are currently pending. Claims 3 and 5 have been amended. Support for those amendments can be found throughout the specification, for example at p. 2, lines 1-5 and p. 3, second to last paragraph, to p. 4, second to last paragraph. Accordingly, the amendments do not add new matter.

II. Acknowledgments

Applicants acknowledge and appreciate the Examiner's indication that the Terminal Disclaimer is in proper form, the withdrawal of the double patenting rejection, and the withdrawal of the claim objections of claims 3 and 4.

Applicants also agree with the Examiner's conclusion that there was only one PTO SB/08 sheet, and appreciate the Examiner's action in changing the erroneous indication of "1 of 2" to "1 of 1."

III. Claim Rejections

A. Rejections under 35 U.S.C. § 112, First Paragraph

Claims 3 and 5 are rejected under 35 U.S.C. § 112, first paragraph, "because the specification, while being enabling for a method of reducing mortality resulting from congestive heart failure in a patient suffering therefrom, does not reasonably provide enablement for reducing the mortality, in general, of a patient suffering from congestive heart failure." Office Action, p. 3.

Applicants have amended the claims as the Examiner suggests (Office Action, p. 3) to recite methods for reducing mortality caused by congestive heart failure in a mammal suffering from congestive heart failure, which the Examiner admits are enabled by the specification. Accordingly, this rejection should be withdrawn.

B. Rejections under 35 U.S.C. § 102

Claims 3 and 5 are rejected under 35 U.S.C. § 102 as being anticipated by Verheugt FWA: Hotline sessions of the 21st European Congress of Cardiology. Eur. Heart J. (1999) 20:1603-1606 ("Verheugt "). The Examiner states that "Verheugt teaches treating congestive heart failure patients with an effective amount of levosimendan, as compared to an effective amount of dobutamine." Office Action, p. 8. The Examiner concludes that, although the reference does not specify the presently claimed the (R)-enantiomer of compound (I), it would have been inherent in the prior art method because of Applicants' disclosure at page 1, the final three lines. Id. at p. 9. Accordingly, Applicants respectfully traverse the present rejection.

Applicants are aware of *Schering Corp. v. Geneva Pharm., Inc.* 339 F.3d 1373 (Fed. Cir. 2003), a case in which the court affirmed the lower court's decision that patent claims were invalid as being inherently anticipated. Applicants submit a copy of that decision herewith for the Examiner's convenience. In that case, a metabolite of an antihistamine loratidine was claimed. However, a prior art patent disclosed administration of loratidine, and the claimed metabolite was known to necessarily and inevitably form from loratidine under normal conditions. Thus, claims to the metabolite were held to be inherently anticipated by the prior art. However, the Court noted that:

> A skilled patent drafter, however, might fashion a claim to cover the metabolite in a way that avoids anticipation....The patent drafter could also claim a method of administering the metabolite or the corresponding pharmaceutical composition.

Id. at 1381.

Here, the claims are drawn to methods comprising administering a pharmaceutical composition comprising an effective amount of the (R)-enantiomer of N-[4-(1,4,5,6-tetrahydro-4-methyl-6-oxo-3-pyridazinyl)phenyl]acetamide (I). In contrast, Verheugt only discloses the administration of levosimendan. Accordingly, the rejection should be withdrawn.

C. Claim rejection under 35 U.S.C. § 103

Claims 3 and 5 are rejected under 35 U.S.C. § 103 as being obvious over Haikala et al (U.S. RE38,102, "Haikala '102"), Haikala et al. (U.S. Patent No. 5,905,078, "Haikala '078"), Applicants' acknowledgment at page 1, lines 2-4 of the third paragraph, or Sircar (U.S. Patent No. 4,397,854, "Sircar") in view of Campbell (U.S. Patent No. 4,432,979, "Campbell") and Diamond et al. (U.S. Patent No. 4,517,310, "Diamond") for reasons stated in the Office Action dated January 27, 2006, further in view of Verheught.

In the January 27, 2006, Office Action, the Examiner stated that Haikala '102, Haikala '078 or Sircar teach racemic N-[4-(1,4,5,6-tetrahydro-4-methyl-6-oxo-3-pyridazinyl)phenyl]acetamide as an effective cardiotonic agent effective for treatment or prevention of congestive heart failure. Office Action dated January 27, 2006, page 4. The Examiner also asserted that Applicants acknowledge, at page 1, lines 3-4 of the

second paragraph of the specification, that the acetamide compound was known for the treatment of chronic heart failure. *Id.* Although, the Examiner conceded that none of those references teaches mortality reduction, he concluded that it would have been obvious to one of ordinary skill in the art to expect a compound which is effective against a disease that can cause mortality would decrease the incidence of mortality.

In the present Office Action, the Examiner states that he is not persuaded that compound (I) was recognized as being an inotropic agent whose actions mirrored the inotropes known at that time. Present Office Action at page 10. He states that, in view of the newly cited Verheugt article, it would appear that one would have expected that the presently claimed (R)-enantiomer of compound (I) was not detrimental to mortality in congestive heart failure patients. Id. Applicants respectfully traverse the rejection.

For the reasons already of record, Applicants submit that none of the cited references suggest that administering a pharmaceutical composition comprising an effective amount of compound (I) would be useful for reducing mortality caused by congestive heart failure. And Verheugt fails to remedy the deficiencies of those references.

For example, Verheugt does not disclose a pharmaceutical composition comprising an effective amount of the (R)-enantiomer of N-[4-(1,4,5,6-tetrahydro-4-methyl-6-oxo-3-pyridazinyl)phenyl]acetamide (I). Verheugt also fails to disclose data sufficient to assess the effect of the (R)-enantiomer of compound (I) on mortality. Specifically, Verheught is silent as to how the mortality curves for levosimendan and dobutamine groups diverged during the period when the (R)-enantiomer of compound (I) was actually present in the plasma of the patient, namely during the period between

days 1 and 13 after administration. See Fig. 1 of the present application, showing that that period corresponds to the period when the (R)-enantiomer of compound (I) was present in patients' plasma after disappearance of the parent drug, levosimendan.

Accordingly, the Examiner has failed to show that any of the cited references, alone or in combination, suggests any mortality reducing effect of the (R)-enantiomer of compound (I) in patients suffering from congestive heart failure. The withdrawal of these rejections is thus respectfully requested.

The Examiner has also challenged that the mortality reducing effect of the (R)-enantiomer of compound (I) in congestive heart failure patients was unexpectedly found in clinical trials conducted by Applicants. Present Office Action at page 10. Applicants respectfully direct the Examiner's attention to Figure 2 of the present specification, which shows a significant divergence of Kaplan-Meyer mortality curves, in favor of levosimendan group as compared to dobutamine, during the period between days 1 and 13. As shown in Fig. 1 and as discussed above, that period corresponds to the period when the (R)-enantiomer of compound (I) was present in patients' plasma after disappearance of the parent drug, levosimendan. Thus, Figs. 1 and 2 suggest that the (R)-enantiomer of compound (I) is capable of producing a significant mortality-reducing effect in patients suffering from congestive heart failure.

IV. Conclusion

In view of the foregoing amendments and remarks, Applicants respectfully request reconsideration and reexamination of this application and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to our Deposit Account 06-0916.

Respectfully submitted,

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Dated: March 21, 2007

By: _____
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Limited Rec. No. L0213